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Development and Characterization of *Tinospora cordifolia* extract Loaded Transethosomal Gel for Topical use

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ABSTRACT

The aim of this study was to formulate and evaluate transethosomes containing *Tinospora cordifolia* for the treatment of arthritis. *Tinospora cordifolia*, known for its properties, was encapsulated in transethosomes to enhance its bioavailability and therapeutic efficacy. The transethosomes were prepared using a thin-film hydration method and characterized for vesicle size, and drug release profile. The optimized formulation exhibited suitable vesicle size, high entrapment efficiency, and a sustained drug release profile. The transethosomal formulation of *Tinospora cordifolia* thus presents a promising alternative for arthritis treatment, offering enhanced delivery and efficacy. Further clinical studies are warranted to confirm its potential therapeutic benefits.

Keywords: Transethosomes; Vesicle size; Drug release profile; Optimized; *Tinospora cordifolia*; Therapeutic benefits; Sustained drug release; Therapeutic efficacy; Bioavailability; Arthritis.

1. Introduction

Oral administration is presently the most common way of medicine delivery. While this has the advantage of being simple to administer, it also has a number of drawbacks, including poor bioavailability due to hepatic metabolism (first pass) and the potential for rapid blood level spikes (both high and low), necessitating high and/or frequent dosing, which can be both costly and inconvenient [1],[3]. Continuous intravenous infusion is seen to be a superior mode of drug administration, not only because it avoids hepatic "first pass" metabolism, but also because it keeps the drug level in the body steady and long-lasting. However, this entails the patients' hospitalization and medical surveillance by the administration [2],[5]. Simultaneously, the transdermal technique offers some advantages over conventional delivery methods, including lower plasma drug levels volatility, gastrointestinal side effects, and high patient compliance [4].

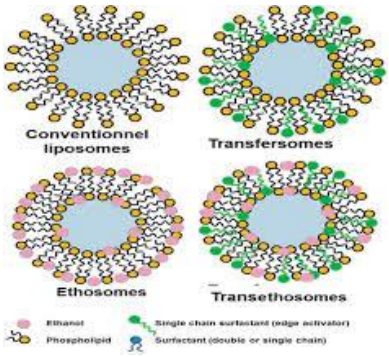

Figure 1. Transethosome [1]

1.1. Study Objectives

The following are the main objectives of this study: (1) Formulate a gel containing *Tinospora cordifolia* stem extract as the active ingredient. (2) Optimize the formulation parameters to enhance the stability. (3) Formulating

the pH of the gel. (4) Evaluate the viscosity of the gel. (5) Determining the spredability and extrudability of the gel. (6) In Vitro drug release studies. (7) DCS study and FTIR.

2. Experimental work

2.1. Pre-formulation study

2.1.1. Plant extract

Tinospora cordifolia stem extract were purchase from market.

2.1.2. Scanning Electron Microscopy (SEM)

The structure of the optimized formulation was examined by SEM at a resolution of 1 and 15 µm. The spherical-shaped vesicles were dominant in the formulation while irregular shapes were limited.

2.1.3. Study of drug-excipient interactions

Using a Fourier-Transform I.R spectrophotometer, the drug and its excipients were examined. By interpreting I.R. spectrums, the drug's interaction with the excipients was found [6],[7].

2.1.4. Solubility Studies

The spontaneous interaction of two or more substance to form homogeneous molecular dispersion is called as solubility [5],[13].

2.2. Formulation of Transethosome

Figure 2. Transethosome Gel

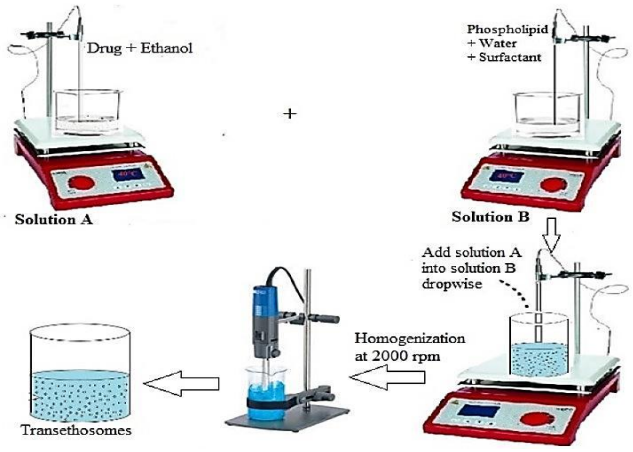

Figure 3. Formulation of Transethosome [1]

Table 1. Chemical use in Transethosome

S. No.	Chemical Name	Use (w/w)		
		F- 01	F- 02	F- 03
01	EXTRACT	0.05gm	0.05gm	0.05gm
02	TWEEN 80	15ml	20ml	5ml
03	SPAN 80	15ml	5ml	20ml
04	ETHANOL	50ml	50ml	50ml
05	WATER	30ml	30ml	30ml
06	SOLY ESTHENE	1gm	0.2gm	0.3gm
07	CARBOPOL	1.5gm	1.5gm	1.5gm
08	EDTA	0.005gm	0.005gm	0.005gm
09	TRI ETHANOL AMINE	q.s	q.s	q.s

2.3. Characterization of Transethosome Gel

2.3.1. Determination of viscosity

Viscosities of the gels were determined by using Brookfield Viscometer. Spindle type, RV-7 at 20 rpm. 100gm of the gel was taken in a beaker and the spindle was dipped in it and rotated for about 5 minutes and then reading was taken [7],[9].

2.3.2. Extrudability

Measuring the force needed to extrude the material from the tube is a helpful empirical test. The formulations were put into collapsible metal tubes with a 5 mm nasal tip whole. The quantity of gel that extruded from the tip of the tube when pressure was applied was used to measure the extrudability of the tube. The formulation's extrudability was examined, and the outcomes were recorded [10],[11].

2.3.3. Spredability

Two sets of glass slides of standard dimensions were taken. The herbal gel formulation was placed over one of the slides. The other slide was placed on the top of the gel, such that the gel was sandwiched between the two slides in an area occupied by a distance of 7.5 cm along the slides. Hundred g weight of gel was placed on the upper slides so that the gel was between the two slides was pressed uniformly to form a thin layer. The weight was removed and the excess of gel adhering to the slides was scrapped off. The two slides in position were fixed to a stand without slightest disturbance and in such a way that only upper slides to slip off freely by the force of weight tied on it. Weight was tied to the upper slide carefully. The time taken for the upper slide to travel the distance of 7.5 cm and separated away from the lower slide under the influence of the weight was noted. The experiment was repeated for

three times and the mean time was taken for calculation. Spreadability was calculated by using the following formula:

S=M*L/T (1)

2.3.4. In Vitro Drug Release

2.3.4.1. Diffusion Study for Transethosome

Using the open-ended cylinder technique, the in vitro release of extract of Tamarindus Indica from the Transethosome formulations was investigated. The glass tube used in this diffusion cell device has an inner diameter of 2.5 cm and is open on both ends. One end is used as a donor compartment and is linked with an artificial membrane.

The purpose of this investigation is to ascertain the penetration rate. The formulations were optimized using data from in vitro tests and the time required to achieve permeation flow in a steady state. Using the in vitro diffusion technique, studies of drug release from transethosome gel formulations were conducted at 37 °C and 100 rpm for a duration of 24 hours. Poured into the glass cell, a weighed quantity of the manufactured transethosome gel formulation was allowed to diffuse against phosphate buffer pH 6.4, which served as the diffusion medium. Using phosphate buffer pH 6.4 as a blank, aliquots were obtained at regular intervals and subjected to spectrophotometric analysis at 290 nm [12].

2.3.5. Stability Study

Three groups of the prepared Transethosome gels were formed. These three Transferosomel gel formulation groups were placed within collapsible aluminum tubes and kept at: Temperature of the room (25 ℃), 40 ℃, and 4 ℃.

For three months, the Transethosome gel formulation was kept in storage. For a duration of three months, samples were taken out each month and their drug content evaluated. They were assessed for physical parameters and product integrity at the conclusion of the third month.

2.3.5.1. Physical evaluation

The physical factors that were taken into account for the assessment were the product's nature, extrudability, pH, viscosity, leak, and phase separation [12],[13].

3. Results and Discussion

3.1. Pre-formulation study

3.1.1. Drug-Excipients interaction study

❖The drug plant extract and the excipients namely Soya lecithin, carbopol, Cholesterol were analyzed by FT-IR spectrophotometer.

❖The FT-IR spectrums were interpreted and it is shown there is no interaction between the drugs with the excipients was conformed [12],[13].

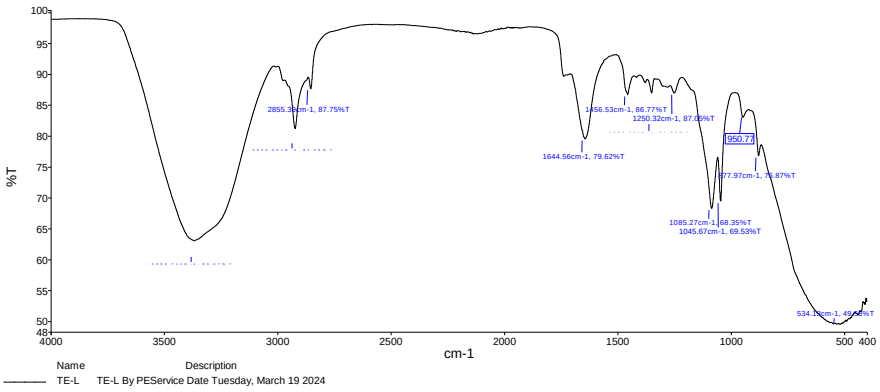

Figure 4. FT-IR of Transethosome

Table 2. FT-IR interpretation of Transethosome

S.No.	Peak Position	Group
01	3369.71	O-H stretching, N-H stretching
02	2924.65	O-H stretching, N-H stretching, C-H stretching
03	2855.39	O-H stretching, N-H stretching, C-H stretching
04	1644.56	C=O stretching, C=N stretching, C=C stretching, N-H bending
05	1456.53	C-H bending
06	1360.24	O-H bending, C-F stretching, S=O stretching
07	1250.32	C-F stretching, C-O stretching, C-N stretching
08	1085.24	C-F stretching, C-O stretching, C-N stretching
09	1045.67	C-F stretching, C-N stretching, S=O stretching, CO-O-CO stretching
10	577.97	C-Cl stretching, C-Br stretching, C-I stretching
11	534.19	C-Br stretching, C-I stretching

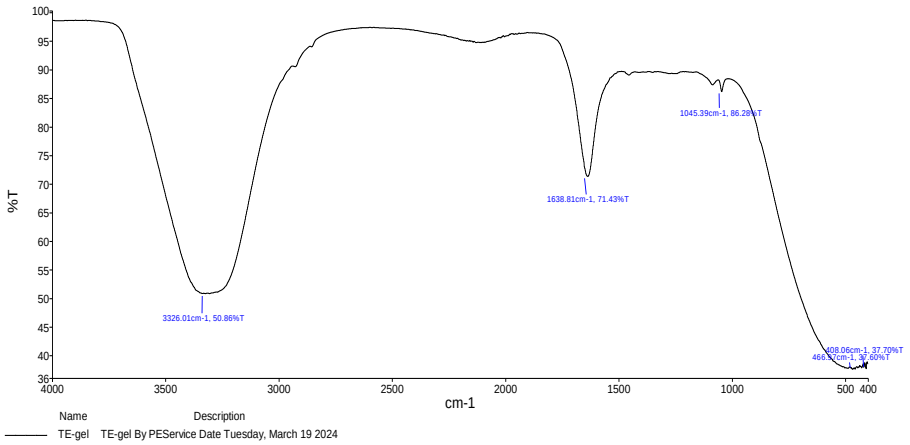

Figure 5. FT-IR of Transethosomal gel

Table 3. FT-IR interpretation of Transethosomal gel

S.No.	Peak Position	Group
01	3326.61	O-H stretching, N-H stretching, C-H stretching
02	1638.81	C=O stretching, C=C stretching, N-H bending
03	1045.39	C-F stretching, C-N stretching, S=O stretching, CO-O-CO stretching

3.1.2. DSC Study

The test was performed "to determine the drug's purity and compatibility with the emulgel formulation and the DSC measurements were carried out using a thermal analyzer and a differential scanning calorimeter (DSC 822 c, Mettler Toledo) here, 2 mg of tretinoin was placed in a sealed aluminium pan and heated at a scanning rate of 50 ºC /min from 20 ºC to 250 ºC under a nitrogen flow of 20 ml/min". As a guide, an empty aluminium pan was employed.

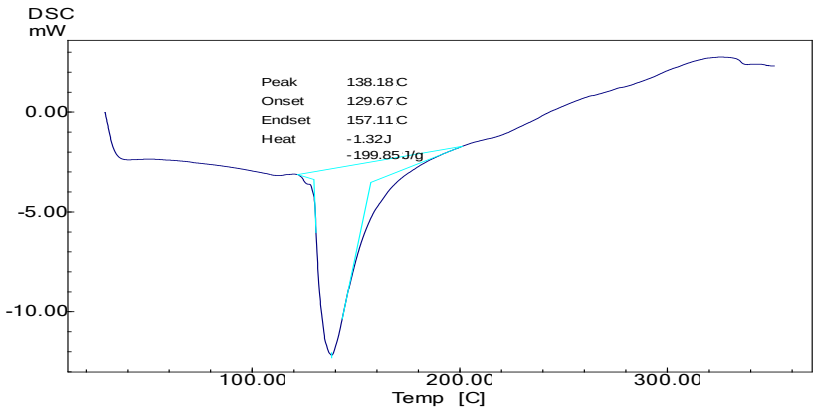

Figure 6. DSC OF Giloy

3.1.3. Solubility Studies

Table 4. Solubility of Giloy

S.No.	Chemical Name	Result
01	Methanol	+++
02	Ethanol	++++
03	Ether	++++
04	Water	++

3.1.4. Transfersomes Evaluations

Scanning Electron Microscopy (SEM)

The structure of the optimized formulation was examined by SEM at a resolution of 1 and 15 µm.

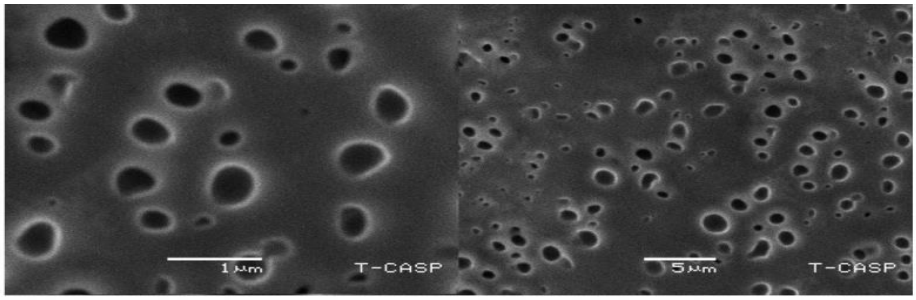

Figure 7. Scanning Electron Microscopy

3.2. Transfersomes Gel Evaluations

3.2.1. Determination of viscosity

The viscosity of the gels was determined by using Brookfield viscometer. The viscosity of the formulations were ranged from 46,000 to 50,000 cps and the results were shown in Table 5.

Table 5. Viscosity Test

S.No.	Formulation	Viscosity in cps
01	Formulation-1	48,000
02	Formulation-2	48,500
03	Formulation-3	46,994

3.2.2. Extrudability

The extrudability of the gel formulations were checked as per the procedure, extrudability of gels was excellent. It is shown in Table 6.

Table 6. Extrudability Test

S.No.	Formulation	Extrudability
01	Formulation-1	+++
02	Formulation-2	+++
03	Formulation-3	+++

3.2.3. Spredability

Table 7. Spredability of Formulation no. 1.

S.No.	Formulation -01	Result
01	Test-01	20±31
02	Test-02	19±31
03	Test-03	21±31

Table 8. Spredability of Formulation no. 2

S.No.	Formulation -02	Result
01	Test-01	24±31
02	Test-02	25±31
03	Test-03	26±31

Table 9. Spredability of Formulation no. 3

S.No.	Formulation -03	Result
01	Test-01	23±31
02	Test-02	19±31
03	Test-03	24±31

Table 10. Spredability Test

S.No.	Formulation	Result
01	Formulation-01	20±31
02	Formulation-02	25±31
03	Formulation-03	22±31

3.2.4. In Vitro Drug Release

Diffusion Study for Transfersomes

Table 11. Drug Release Test

S.No.	Time in (hrs)	Absorbance at 290 nm
1	0	0
2	0.25	0.627
3	0.5	0.648
4	0.75	0.656
5	1	0.659
6	1.5	0.662
7	2	0.668
8	2.5	0.669

9	3	0.671
10	4	0.674
11	5	0.678
12	6	0.686
13	7	0.688
14	8	0.689
15	9	0.694
16	10	0.696
17	11	0.698
18	12	0.699
19	14	0.703
20	16	0.709
21	18	0.715
22	20	0.717
23	22	0.718
24	24	0.718

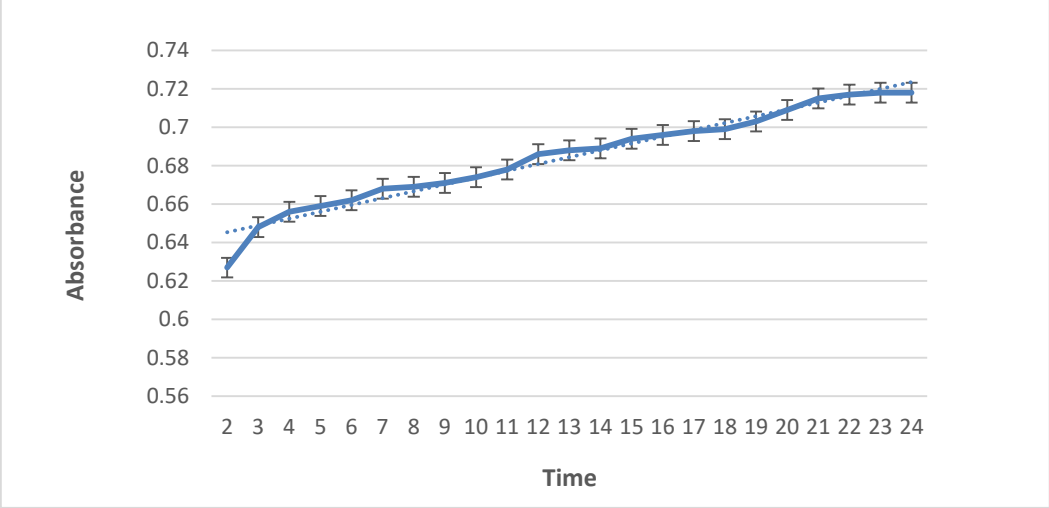

Figure 8. Drug Release Test

3.2.5. Stability Study

The stability studies of formulation were carried out at refrigeration temperature (4 °C), Room temperature and 40 °C. Physical evaluation of prepared formulation shown in the Table no. 12

Table 12. Stability Study

Parameter	Room Temperature (25 ℃)	40 ℃	4 ℃
Visual Appearance			
• Initial	Green colour gel	Green colour gel	Green colour gel
• 1 month	Green colour gel	Green colour gel	Green colour gel
• 2 month	Green colour gel	Green colour gel	Green colour gel
• 3 month	Green colour gel	Green colour gel	Green colour gel
pH			
• Initial	6.7	6.7	6.7
• 1 month	6.7	6.7	6.7
• 2 month	6.8	6.8	6.8
• 3 month	6.8	6.8	6.8
Viscosity			
• Initial	48,500	48,500	48,500
• 1 month	48,500	48,500	48,500
• 2 month	48,497	48,497	48,500
• 3 month	48,495	48,495	48,497
Extrudability			
• Initial	Satisfactory	Satisfactory	Satisfactory
• 1 month	Satisfactory	Satisfactory	Satisfactory
• 2 month	Satisfactory	Satisfactory	Satisfactory
• 3 month	Satisfactory	Satisfactory	Satisfactory
Phase Separation			
• Initial	Not found	Not found	Not found
• 1 month	Not found	Not found	Not found
• 2 month	Not found	Not found	Not found
• 3 month	Not found	Not found	Not found
Texture			
• Initial	Smooth	Smooth	Smooth
• 1 month	Smooth	Smooth	Smooth
• 2 month	Smooth	Smooth	Smooth
• 3 month	Smooth	Smooth	Smooth

4. Conclusion

This study successfully formulated and evaluated transethosomes containing *Tinospora cordifolia* for the treatment of arthritis. The optimized transethosomal formulation demonstrated suitable vesicle size, and sustained drug release, resulting in enhanced bioavailability. These findings suggest that the transethosomal delivery system effectively enhances the therapeutic potential of *Tinospora cordifolia*, making it a promising alternative for arthritis treatment. Further clinical investigations are recommended to validate these results and confirm its therapeutic benefits in human subjects.

5. Summary

The study focused on developing and evaluating transethosomes containing *Tinospora cordifolia* for arthritis treatment. Utilizing a thin-film hydration method, the transethosomes were formulated and characterized for key parameters such as vesicle size, and drug release profile. The optimized formulation showed promising characteristics, including high entrapment efficiency and sustained drug release. The findings indicate that transethosomal delivery of *Tinospora cordifolia* enhances its therapeutic potential, offering a promising alternative for arthritis management. Further clinical research is suggested to confirm its efficacy in human subjects.

6. Future Prospects of *Tinospora cordifolia* Extract Loaded Transethosomal Gel for Topical Use

Enhanced Drug Delivery and Efficacy

Future research could focus on optimizing the formulation to enhance the bioavailability and therapeutic efficacy of *Tinospora cordifolia* extract. This includes fine-tuning the size and stability of transethosomes to ensure deeper skin penetration and prolonged drug release.

Broad-Spectrum Applications

Tinospora cordifolia has known anti-inflammatory, antioxidant, and immunomodulatory properties. Future studies can explore its potential applications in treating a wider range of skin conditions such as psoriasis, dermatitis, and wound healing, leveraging its broad-spectrum therapeutic effects.

Clinical Trials and Safety Profiling

Extensive clinical trials are necessary to validate the safety and efficacy of the transethosomal gel in humans. This would involve assessing potential side effects, optimal dosage, and long-term effects to ensure the formulation is safe for widespread use.

Customization and Personalization

Advances in personalized medicine could allow for the development of customized transethosomal gels tailored to individual patient needs. This could involve adjusting the concentration of *Tinospora cordifolia* extract or combining it with other active ingredients based on specific skin conditions or patient profiles.

Commercialization and Market Potential

With positive clinical outcomes, there is significant potential for commercializing *Tinospora cordifolia* extract loaded transethosomal gel. The formulation could be developed into various product lines such as anti-aging

creams, acne treatments, and general skincare products, tapping into the growing demand for natural and effective topical treatments.

Declarations

Source of Funding

This study did not receive any grant from funding agencies in the public, commercial, or not-for-profit sectors.

Competing Interests Statement

The authors declare no competing financial, professional, or personal interests.

Consent for publication

The authors declare that they consented to the publication of this study.

Authors' contributions

All the authors took part in literature review, analysis and manuscript writing equally.

Availability of data and material

All data pertaining to the research is kept in good custody by the authors.

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